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(CASE REPORT)

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No reflow phenomenon: Insights from 10 case reports

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Abstract

The no-reflow phenomenon refers to inadequate perfusion of a part of the myocardium located downstream of an epicardial artery. It affects 5 to 30% of patients who have undergone reperfusion via angioplasty. Since this phenomenon significantly limits the benefits of reperfusion and is a poor prognostic factor, several studies have focused on analyzing the various pathophysiological mechanisms, which remain a current topic of interest. Its diagnosis relies on a combination of clinical findings, electrocardiogram, coronary flow after angioplasty, and cardiac imaging using MRI. Although medical treatment may improve prognosis, prevention remains the most effective therapeutic approach. Our study reports the experience of our department through 10 clinical cases of no-reflow during primary coronary angioplasty in the context of acute coronary syndrome with ST-segment elevation, along with a literature review.

Objective of study: The objective of this study is to review the pathophysiology, predictive factors, and diagnostic and therapeutic approaches to the no-reflow phenomenon, by presenting ten clinical cases illustrating this phenomenon in the context of ST-elevation myocardial infarction

Material and methods: This retrospective study, conducted from June 2021 to March 2023 at the Military Hospital of Rabat, included STEMI patients who underwent primary angioplasty and developed the no-reflow phenomenon. Criteria for inclusion included significant flow reduction, failure to reperfuse, high thrombotic burden, persistent ST elevation, and lack of LV function improvement. Ten patients met the criteria after reviewing medical records.

Conclusion: No-reflow is common during the acute phase of myocardial infarction and is an important marker of mortality. Despite the reopening of the culprit artery, distal microcirculation is often impaired. Its pathogenesis is complex and multifactorial. At-risk patients can be identified through simple clinical and angiographic criteria, such as age, delayed recanalization, low TIMI flow, high thrombotic burden, and long lesions. No single therapy is sufficiently effective, and a combined approach involving multiple strategies and addressing risk factors is necessary. Several treatment options are currently under investigation.

Keywords: No reflow; Primary angioplasty; Acute coronary syndrome with ST-segment elevation (STEMI); Coronary flow

1. Introduction:

The reference technique in the management of acute coronary syndrome with ST-segment elevation is mechanical reperfusion of the occluded coronary artery through urgent primary angioplasty. [1] Although the success rate of this standard technique is approximately 95%, the no-reflow phenomenon limits its benefit and serves as an independent predictive factor for heart failure, rehospitalization, recurrence of acute coronary syndrome, and even death. [2, 3] Early

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diagnosis of no-reflow is therefore crucial, as it enables the implementation of preventive strategies—particularly the use of quadritherapy (aspirin, clopidogrel, heparin, and glycoprotein IIb/IIIa inhibitors)—which have been shown to reduce its incidence and improve clinical outcomes. Preventing its occurrence after angioplasty requires a thorough understanding of its mechanisms and pathophysiology, which have recently been the subject of several research studies. In this context, we review the pathophysiology, predictive factors, and diagnostic and therapeutic approaches to no-reflow in relation to ten patients admitted to the cardiology department at the Mohamed V Military Hospital in Rabat.

2. Materials and methods

This is a retrospective study conducted over a period of 21 months, from June 2021 to March 2023, in the intensive care units of the cardiology center at the Military Hospital of Rabat. We included patients who were admitted for acute coronary syndrome with ST-segment elevation (STEMI) and underwent primary angioplasty with suspected no-reflow post-angioplasty. The patients included in the study exhibited criteria during follow-up indicating the no-reflow phenomenon, including significant flow reduction, failure to reperfuse the affected artery, high thrombotic burden, deep and wide Q waves in the infarct territory, persistent ST-segment elevation, and lack of improvement in left ventricular (LV) function. We excluded patients who were admitted outside the revascularization time window or who had a successful primary angioplasty, defined as the disappearance of pain, regression of the ST segment, normal flow in the culprit artery, and improvement in LV function. Data collection, conducted through an exhaustive search of medical records, identified 10 patients who met these criteria.

3. Results

Upon admission, all patients underwent a complete clinical examination, an 18-lead electrocardiogram, and echocardiography, and were urgently transferred to the catheterization lab for primary angioplasty. Following angioplasty, monitoring included a follow-up ECG and assessment of ventricular function.

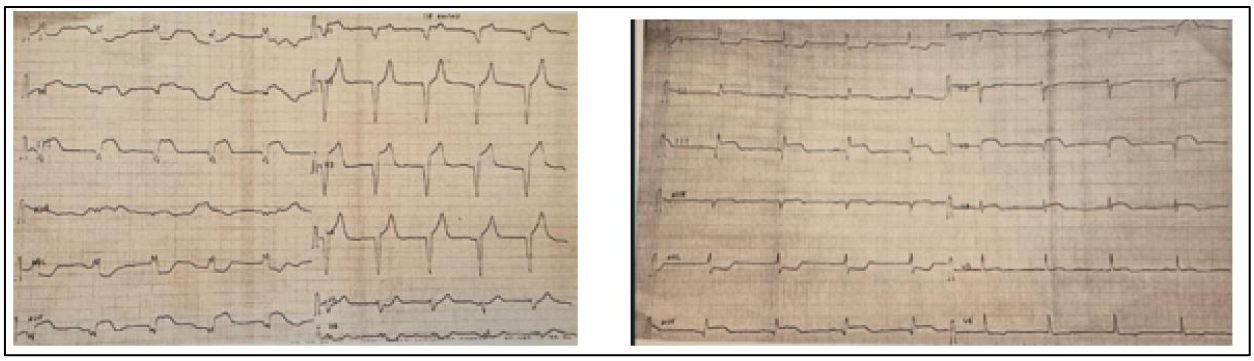

Figure 1 Electrocardiogram of Patient No. 1, before and after angioplasty

Figure 2 Coronary angiography images taken at 6 hours post-procedure of Patient No. 1

3.1. Predictive factors of no reflow

As the predictive factors for no reflow include age, sex, diabetes, smoking, reperfusion delay, culprit artery diameter, lesion location, and TIMI flow prior to angioplasty, we summarize the parameters of our patients in FIGURE 3.

Table 1 Predictive factors recorded in the patients

Patient	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Age (years)	70	84	57	69	37	68	63	40	52	76
Sex	M	M	M	M	M	F	M	M	M	M
Diabetes	+	+	-	+	-	+	-	-	-	-
Smoking	+	+	+	-	+	+	-	+	+	-
Dyslipidemia	-	-	-	-	-	-	+	-	+	-
Reperfusion delay	H6	H6	H4	H15	H4	H5	H6	H5	H6	H6
Lesion location	RCA	RCA	Cx	LAD	LAD	LAD	RCA	LAD	RCA	LAD
TIMI flow before angioplasty	TIMI 1	TIMI 0	TIMI 0	TIMI 0	TIMI 0	TIMI 0	TIMI 0	TIMI 1	TIMI 0	TIMI 0

Although the average age of our patients is 61.1 years, ischemic heart disease also affects young individuals with its specific characteristics. We observed two young patients in our series, aged 37 and 40 years.

The average age of patients in our study is 61.1 years, with 2 young patients aged 37 and 40 years, showing a clear male predominance, with 90% of patients being male. The occurrence of this phenomenon in young patients is closely associated with heavy smoking and sometimes a family history of coronary artery disease. This is the case in our study, where the common denominator between these two patients is smoking. Regarding the topography of myocardial infarction in young patients, both of these patients had single-vessel disease involving the left anterior descending artery (LAD).

Smoking is the predominant cardiovascular risk factor, with 5 smokers in our series. Based on our study, we can establish a correlation between no-reflow and smoking, while also emphasizing the young age of these patients (median age of 59 years). In our series, we observe a male predominance, with 9 men and only one woman.

Diabetes is known to be an important predictive factor for mortality in coronary patients. In our study, due to the limited number of cases, we were unable to establish a statistically significant correlation between no-reflow and diabetes, as only 3 out of 10 patients were diabetic.

One of the major issues related to the no-reflow phenomenon is reperfusion time. The longer the reperfusion delay, the less likely TIMI III flow is to be restored, due to the thrombus becoming firmer.

Our study demonstrates a link between delayed revascularization and the risk of no-reflow, as all patients presented to the hospital more than 240 minutes after the presumed onset of pain. Regarding the location of coronary obstruction, it is interesting to note that none of the locations can predict future myocardial perfusion. Indeed, an infarction caused by obstruction of a proximal trunk is not significantly correlated with the presence of no-reflow. However, involvement of the left anterior descending artery at its proximal and mid-portions clearly appears in our series as an important predictive factor for poor myocardial reperfusion. In our study, 2 patients were admitted with TIMI 1 flow, and 8 patients with TIMI 0 flow in the culprit artery before primary coronary angioplasty. Preoperative TIMI flow appears to be an independent risk factor for the no-reflow phenomenon in elderly patients with STEMI.

Table 2 Calculation of the risk of no-reflow in our patients over 60 years of age, according to the nomo gram by Li Yang et al

Patient	**1**	**2**	**4**	**6**	**7**	**10**
Preoperative TIMI flow	**TIMI 1 (28)**	**TIMI 0 (28)**	**TIMI 0 (28)**	**TIMI 0 (28)**	**TIMI 0 (28)**	**TIMI 0 (28)**
Target lesion diameter	**< 3,5 mm (0)**	**< 3,5 mm (0)**	**< 3,5 mm (0)**	**< 3,5 mm (0)**	**< 3,5 mm (0)**	**≥ 3,5mm (34)**

Collateral circulation	**Grade 0 (76)**	**Grade 0 (76)**	**Grade 0 (76)**	**Grade 0 (76)**	**Grade 0 (76)**	**Grade 0 (76)**
Pulse pressure (mmHg)	**103 (17)**	**23 (83)**	**53 (58)**	**33 (75)**	**70 (42)**	**54 (58)**
Number of leads with ST elevation	**6 (66)**	**4 (44)**	**5 (55)**	**3 (33)**	**6 (66)**	**3 (33)**
Total score	**187**	**231**	**217**	**212**	**212**	**229**
Risk	**0,3**	**0,5**	**0,4**	**0,4**	**0,4**	**0,5**

Our 6 patients over 60 years of age have a risk within the predicted no-reflow threshold (ranging from 0 to 0.55), based on preoperative TIMI flow, culprit lesion diameter, collateral circulation, pulse pressure, and the number of leads with ST-segment elevation.

3.2. Therapeutic management

In our study, balloon angioplasty alone, which is now only used in certain cases (such as very distal lesions in tortuous or calcified vessels, diffuse lesions in small vessels requiring long and multiple stenting, dilation of a daughter branch, or high thrombotic burden), was performed in 6 patients in our series. It was implemented not only as a therapeutic technique but also as part of a non-pharmacological prevention strategy aimed at preventing no-reflow.

It was performed in Patient No. 1 due to the presence of a thrombotic-appearing lesion in the mid-coronary artery and a significant stenosis in the same artery in its middle segment. In Patients No. 2, No. 4, and No. 6, balloon angioplasty was indicated and preceded by thromboaspiration due to the high thrombotic burden.

In Patient No. 7, balloon dilation was indicated since coronary angiography showed three lesions in the right coronary artery in the proximal, mid, and distal segments. In Patient No. 9, balloon angioplasty was indicated due to the high thrombotic burden, with coronary angiography revealing a lesion in the mid-right coronary artery and acute occlusion in its distal segment with a thrombotic appearance. The placement of a drug-eluting stent was excluded in this case as surgery had been scheduled, which presented a hemorrhagic risk.

The other patients in the series underwent placement of a drug-eluting stent during angioplasty. The choice of stent was based on the following criteria:

- Lesions greater than 15mm
- Vessel diameter less than 3 mm
- Presence of diabetes and/or chronic renal insufficiency
- In-stent restenosis
- Total coronary occlusion

The diagnosis of no-reflow was made based on:

- Slowed flow (TIMI 2 in 7 patients and TIMI 1 in 3 patients)
- Intraluminal thrombus in the culprit artery, indicating a high thrombotic burden in 8 patients
- Persistent ST-segment elevation during follow-up in 7 patients
- No improvement in left ventricular (LV) function after revascularization in 5 patients.

In parallel with revascularization, our patients were treated with tirofiban as an antiplatelet agent, at a dosage of 0.4 micrograms/kg/min for 30 minutes, followed by a continuous infusion at 0.1 micrograms/kg/min for 48 hours. Tirofiban was administered simultaneously with unfractionated heparin, typically as an intravenous bolus of 50-60 IU/kg, followed by approximately 1000 IU to ensure better inhibition of platelet function during the critical initial phase of tirofiban treatment.

In our study, it is worth noting that there was a trend toward an increase in myocardial perfusion on angiography, with a difference in TIMI flow. This regimen ensured better inhibition of platelet aggregation, as observed based on the results, in 7 patients with TIMI 2 flow. In the remaining 3 patients, TIMI 1 flow was achieved. Tirofiban had a positive

effect on ST-segment resolution, with ST-segment resolution observed in 6 patients, indirectly suggesting an improvement in microvascular perfusion.

4. Discussion

No reflow has a prevalence ranging from 5% to 30%, depending on the evaluation method and the population studied. It is observed in 10% of cases of primary coronary angioplasty and in less than 2% in the context of NSTEMI or during elective angioplasty. It is defined as inadequate perfusion of a portion of the myocardium located downstream from a segment of an epicardial coronary artery, which does not exhibit a patent mechanical obstruction. [4]

4.1. Classification of No Reflow

Two types of no reflow are distinguished:

- No reflow after elective angioplasty: This type is unpredictable and occurs suddenly, presenting clinically as acute ischemia with chest pain and electrical changes. It is associated with a high rate of myocardial infarction and mortality. [5]
- No reflow after primary angioplasty in STEMI: Present in 30% of patients who have undergone primary angioplasty. It is confined to the irreversibly damaged necrotic area and may be exacerbated during reperfusion. Clinically, it can manifest as persistent chest pain with no resolution of ST-segment elevation on the ECG. It is an independent predictor of adverse clinical outcomes after an ACS and is associated with increased mortality. [6]

4.2. Pathophysiology

Microvascular obstruction is the underlying pathophysiological mechanism of no reflow. Microvascular obstruction and no reflow, after reperfusion of an occluded coronary artery, are explained by the combined action of at least four factors:

- **Myocardial ischemia**: A vascular injury process responsible for prolonged ischemia leads to cellular dysfunction in the myocardium, which may progress to cell death. The damage is initially reversible but becomes irreversible and affects not only the endothelial cells, whose protrusions obstruct the microcirculation, but also vascular cells [7]. Necrosis of endothelial cells results in extravasation and impaired nitric oxide production, which in turn affects endothelium-dependent vasodilation [7,8]. This aspect of microcirculation likely plays a major role in the onset of no reflow.
- **Distal embolization**: The embolization of atherosclerotic plaque thrombotic fragments occurs spontaneously or during primary coronary angioplasty, following guidewire passage, lesion preparation, and stent implantation. It is visible angiographically in 11 to 17% of STEMI cases treated with primary angioplasty [9,10], though its actual incidence is higher [11]. Distal embolization is more frequent in large-volume plaques and those with greater thrombus at the lesion site [12,13,14]. Additionally, thrombi rich in erythrocytes, high blood glucose levels at admission, a larger culprit vessel, balloon pre-dilation, and involvement of the right coronary artery have been identified as independently associated with a higher risk of distal embolization during the procedure [10,15].
- Since these microthrombi preferentially embolize into well-reperfused, viable myocardium, they lead to necrosis of potentially salvageable myocardial tissue [16]. This phenomenon contributes to no reflow through both mechanical obstruction and an increase in vasoconstrictive tone at the arteriolar level and within the microcirculation [17,18,19].
- **Reperfusion injury**: Reperfusion of ischemic tissues is often associated with microvascular dysfunction, characterized by impaired endothelium-dependent dilation and leukocyte recruitment [20,21]. This imbalance leads to the production and release of inflammatory mediators (TNF-α, IL-1β, ET-1, and selectins), which appear to play an important role in no reflow [22,23].
- **Individual susceptibility**: There is likely individual variability, as for the same duration of ischemia, not all patients have the same infarct size or prognosis. These differences are not well understood, but collateral circulation and recent pre-infarction angina may play a role. Diabetes and hypercholesterolemia are detrimental to the occurrence of no reflow, as it is more frequent in patients admitted with hyperglycemia, and hypercholesterolemia exacerbates reperfusion injury by increasing endothelial oxidative stress [24,25,26].

4.3. Predictive Factors of No Reflow

The phenomenon of no reflow has a multifactorial pathogenesis. The contributing factors include age, sex, diabetes, smoking, and revascularization delay, the diameter of the culprit artery, lesion location, and TIMI flow before angioplasty.

In the meta-analysis by Gupta [27], an age of 60 years or older was correlated with the presence of no reflow. In the series by M. Chettibi [28], patients with poor myocardial reperfusion were older, with an average age of 59 years (p=0.08). Advanced age is widely recognized as a risk factor for no reflow [29], with the mechanism likely related to microvascular dysfunction and arterial stiffness associated with aging [30,31].

Male sex is also considered one of the predictive factors for no reflow, as demonstrated in studies by Rezkalla SH et al. [32], and Omar F Tawfi et al. [33], where male sex predominated, accounting for 73.2%. There are several potential differences between male and female arteries that could explain this [33]. While limited information exists regarding differences in coronary microcirculation, vascular function differences seem to be influenced by estrogen levels, which have a vasodilatory effect [34].

Primary angioplasty has shown better outcomes compared to fibrinolysis in terms of mortality. However, these two techniques yield nearly the same results in diabetic patients, who have less complete ST-segment resolution than non-diabetic patients after stent placement. Several explanations can account for this: endothelial dysfunction [36], coronary reserve abnormalities [37], and certain microvascular and myocardial structural abnormalities [38,39]. Elevated free fatty acid levels during hyperglycemia reduce vascular motility, and hyperglycemia promotes leukocyte accumulation in the myocardial microcirculation and increases the procoagulant properties of platelets [40,41].

In our study, we found a correlation between no reflow and smoking, which is supported by the study conducted by Arel et al., where a strong relationship was proven. These results await further confirmation in larger primary angioplasty databases [42], as some studies have shown that in STEMI patients undergoing primary angioplasty, active smoking is associated with better myocardial reperfusion than non-smokers [43,44]

One of the parameters associated with the no reflow phenomenon is reperfusion time, as delayed reperfusion can lead to an older and more organized intracoronary thrombus, increasing the risk of distal embolization during primary angioplasty and reducing the likelihood of achieving TIMI 3 flow after the procedure [45,46,47]. However, the use of a distal protection device in this case can improve myocardial reperfusion by mitigating the adverse effects of the organized thrombus [48].

Regarding the location of coronary obstruction, it is interesting to note that no specific location can predict future myocardial perfusion. Indeed, an infarction due to proximal LAD obstruction, or more generally a proximal trunk obstruction, is not significantly correlated with the presence of no reflow. However, involvement of the proximal and mid anterior interventricular artery appears clearly in our series as a predictive factor for poor myocardial reperfusion. Several studies, notably those by De Luca et al. [49] and Zhou et al. [50], have revealed that preoperative TIMI blood flow is an independent risk factor for the no reflow phenomenon in elderly STEMI patients.

Other factors that predict no reflow include the diameter of the culprit lesion, the extent of collateral circulation, pulse pressure, and the number of lead II ST-segment elevations. These factors, along with TIMI flow before angioplasty, were used by Li Yang et al. to develop a nomogram that predicts the occurrence of no reflow in elderly patients [51].

Table 3 Predictive Factors for the No-Reflow Phenomenon

Predictive Factor	**Category**	**Description**
Age ≥ 65 years	Patient-related	Older age is associated with more extensive microvascular dysfunction and a higher risk of no-reflow.
Diabetes mellitus	Patient-related	Chronic hyperglycemia promotes microvascular injury, inflammation, and endothelial dysfunction.
Hypertension	Patient-related	Long-standing hypertension leads to small-vessel remodeling and impaired vasodilatory reserve.
Hyperlipidemia	Patient-related	Elevated LDL and triglycerides contribute to endothelial dysfunction and increased plaque instability.
Smoking	Patient-related	Tobacco use induces vasoconstriction, inflammation, and prothrombotic state, worsening microcirculation.
High platelet count / elevated CRP	Laboratory	Markers of inflammation and platelet activation correlate with microvascular obstruction risk.

Killip class ≥ II at presentation	Clinical	Signs of heart failure on admission (e.g., pulmonary rales, S3 gallop) indicate larger infarct and microvascular damage.
High thrombus burden	Angiographic	Large intracoronary thrombus increases risk of distal embolization and microvascular plugging.
Pre-PCI TIMI flow ≤ 1	Angiographic	Poor or absent antegrade flow before intervention signifies extensive distal bed compromise.
Multivessel coronary artery disease	Angiographic	Presence of additional significant stenoses reduces collateral flow and increases no-reflow likelihood.
Delayed symptom-to-balloon time (> 4 h)	Procedural	Longer ischemic duration leads to more irreversible microvascular injury before reperfusion.
Use of high-pressure balloon inflation	Procedural	Aggressive dilation can dislodge plaque debris, causing microembolization and capillary obstruction.

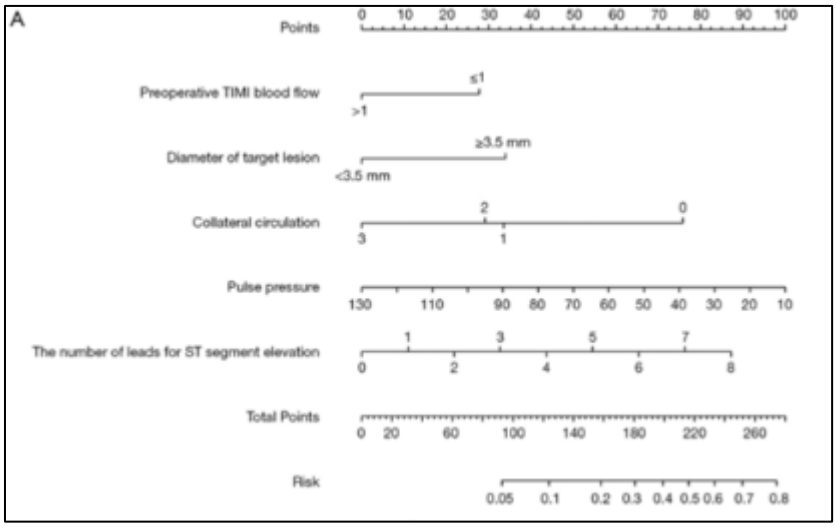

Figure 3 Nomogram to assess the risk of no-reflow after coronary angioplasty in elderly STEMI patients. Adapted from Li Yang et al. [51]

4.4. Diagnosis

The clinical presentation of no-reflow is often characterized by persistent or even worsening pain after reperfusion of the epicardial artery. In severe cases, the clinical presentation may include ventricular arrhythmias or cardiogenic shock, indicating a poor prognosis for no-reflow. In addition to these clinical signs, electrocardiographic changes such as persistent ST-segment elevation or new Q waves can suggest inadequate myocardial reperfusion despite successful opening of the epicardial vessel. These early clinical and ECG findings provide valuable clues for the early detection of no-reflow before confirmation by imaging.

4.4.1. Invasive evaluation by angiography:

The TIMI score is used for the semi-quantitative assessment of the progression of the contrast agent in the epicardial segments of the coronary arteries [52]. It tends to overestimate the impact of revascularization since coronary angiography only provides a rough approach to the coronary microcirculation: only 5% of the myocardial bed is opacified by this method. It lacks both sensitivity and specificity for evaluating no-reflow [53]. The TIMI Frame Count score: This was developed for the semi-quantitative evaluation of myocardial reperfusion using coronary angiography [54,55]. It is a reproducible method with low inter- and intra-observer variability and an excellent correlation with 30-day mortality.

Myocardial Blush Grade (MBG): This method measures myocardial reperfusion by quantifying contrast uptake in myocardial tissue (long angiographic sequences extending to the venous phase) [56]. This method shares the same limitations as the classic TIMI scale [57].

Experts from the GRCI (Group for Reflection on Interventional Cardiology) suggest that microvascular obstruction indicating no-reflow on angiography is present if the TIMI flow is less than 3 and/or the MBG score is 0 or 1 [58].

4.4.2. Non-invasive evaluation

Non-invasive evaluation primarily relies on cardiac MRI, which provides direct assessment of myocardial perfusion and microcirculation [59]. Two distinct approaches are used to diagnose microvascular obstruction using cardiac MRI: First-pass perfusion: No-reflow is defined by a delayed myocardial contrast uptake during the first 3 minutes after gadolinium injection, resulting in a hypointense subendocardial zone on early-phase acquisitions [60]. Late gadolinium enhancement: The no-reflow zone is defined as a hypo-intense area located within the middle of the myocardial infarction on delayed enhancement sequences performed at 3 minutes (late contrast enhancement) or 10 minutes (late contrast enhancement) after iodinated contrast injection, with the hypointense image "sandwiched" between the hyperintense necrotic zone [61]. In addition to being a sensitive and non-invasive test, MRI has the advantage of being able to be performed after some time has passed since the myocardial infarction. No-reflow is a progressive and dynamic phenomenon that may extend up to 48 hours post-myocardial infarction and stabilize after one month. Therefore, it is recommended to wait at least 2 days before performing cardiac MRI after coronary occlusion to avoid underestimating the extension of no-reflow [62,63].

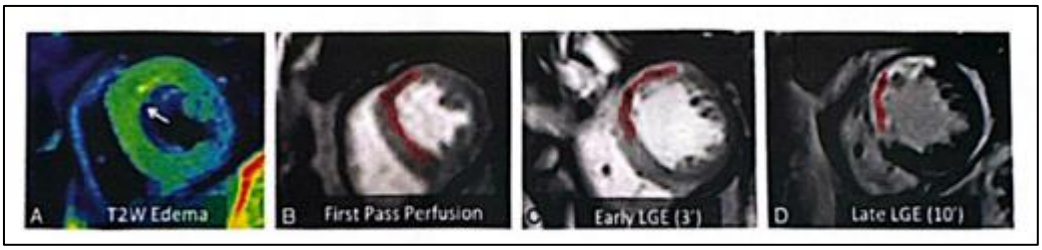

Figure 4 No-reflow phenomenon on cardiac MRI: first-pass perfusion and late gadolinium enhancement [60]

4.5. Therapeutic Approaches:

The management of no-reflow begins with its prevention through predictive factors. Several studies have shown that reducing reperfusion delay, optimal blood glucose control prior to the procedure, and the use of statins before the intervention are associated with a significant reduction in no-reflow. [64, 65, 66, 67] The use of active dual antiplatelet therapy, as well as early anticoagulation with unfractionated heparin during the procedure, can help prevent the risk of no-reflow.
Early recognition of no-reflow is particularly important not only to guide acute management but also to prevent adverse outcomes such as left ventricular (LV) remodeling and heart failure. A prompt diagnosis—based on clinical signs, ECG changes, or angiographic findings—enables the early initiation of an intensified preventive strategy. In this context, the use of quadritherapy (aspirin, clopidogrel, unfractionated heparin, and glycoprotein IIb/IIIa inhibitors) has shown potential in minimizing microvascular obstruction and improving myocardial salvage, thereby reducing the extent of infarct-related injury and mitigating LV remodeling.

General best practices in angioplasty are essential: the use of intracoronary nitrates at the beginning of the procedure, optimal catheter selection, and regular catheter flushing. [68] Balloon angioplasty has beneficial effects by expanding the weakest part of the coronary artery wall. To prevent microembolization of debris during atherectomy, medical treatment should include effective dual antiplatelet therapy, vasodilators, and appropriate medication use. The benefit of antiplatelet therapy has been established with the use of anti-GPIIb/IIIa agents, which reduce procedural morbidity and CK-MB elevation. [69, 70]

Preventive vasodilators are used to reduce slow flows, combining nitrates with calcium channel blockers and sometimes adenosine in the rinse solution with heparin. [71]

Stent placement (guided by imaging) and avoiding high-pressure dilation should be considered, when possible, in STEMI patients at risk for no-reflow. [72]

When no-reflow is suspected, other causes of vascular occlusion, such as dissection, thrombus migration, and vasospasm, should be ruled out through imaging. Once vessel patency is confirmed, vasodilators should be administered generously, therapeutic activated clotting time (ACT) should be ensured, and hemodynamic support should be provided if necessary (e.g., Impella, balloon counterpulsation).

Management includes both pharmacological and non-pharmacological measures. The table below summarizes the main medications used in the management of no-reflow. [73]

Mechanical treatment relies on post-conditioning through repeated inflations of an angioplasty balloon upstream of the culprit lesion immediately after reperfusion, which significantly reduces the extent of no-reflow. Thrombectomy prior to coronary angioplasty is also associated with improved clinical outcomes in patients with STEMI.

Table 4 Main Medications and Doses for the Treatment of No-Reflow. Adapted from Annibali et al. [74]

Medication	**Dosage**	**Dilution (concentration)**	**Side Effects**
Adenosine	Intravenous: 70 µg/kg/min Intracoronary: 100-200 µg bolus	2 mg diluted in 4 mL of normal saline → 0.5 mg/mL	Bradycardia, hypotension, chest pain, dyspnea
Sodium nitroprusside	Intracoronary: 60-100 µg bolus	50 mg diluted in 250 mL of normal saline → 200 µg/mL	Bradycardia and hypotension
Verapamil	Intracoronary: 100-500 µg bolus (max: 1 mg)	5 mg diluted in 10 mL of normal saline → 0.5 mg/mL	Bradycardie, bloc cardiaque transitoire
Diltiazem	Intracoronary: 400 µg bolus (max: 5 mg)	5 mg diluted in 10 mL of normal saline → 0.5 mg/mL	Bradycardia, hypotension
Nicardipine	Intracoronary: 200 µg bolus (max: 1 mg)	2.5 mg diluted in 10 mL of normal saline → 0.25 mg/mL	Bradycardia, hypotension
Epinephrine	Intracoronary: 80-100 µg bolus	1 mg diluted in 10 mL of normal saline → 0.1 mg/mL	Malignant arrhythmias
Nicorandil	500 µg (max : 5 mg)	2 mg diluted in 10 mL of normal saline → 0.2 mg/mL	Malignant arrhythmias
Streptokinase	250 kU over 3 min	250,000 U diluted in 50 mL of normal saline → 5,000 U/mL	Bleeding
Tenecteplase	5 mg (max : 25 mg)	50 mg diluted in 10 mL of normal saline → 5 mg/mL	Bleeding
Tissue plasminogen activator (tPA)	0,025 – 0,5 mg/kg/h	10 mg diluted in 10 mL of normal saline → 1 mg/mL	Bleeding
Abciximab	0.25 mg/kg bolus, then 0.125 µg/kg/min (max 10 µg/min) infusion for 12 hours	10 mg diluted in 10 mL of normal saline → 1 mg/mL	Bleeding
Eptifibatide	180 µg/kg bolus, then 180 µg/kg bolus 10 minutes later, followed by 2 µg/kg/min infusion until 18 hours If CrCl < 50 ml/min: reduce infusion by 50%	20 mg diluted in 10 mL of normal saline → 2 mg/mL	Bleeding
Tirofiban	25 µg/kg over 3 minutes, then 0.15 µg/kg/min infusion until 18 hours If CrCl < 30 ml/min: reduce infusion by 50%	25 mg diluted in 250 mL of normal saline → 0.1 mg/mL	Bleeding

5. Conclusion

In conclusion, no reflow is a common phenomenon during the acute phase of myocardial infarction and represents an important marker of mortality. Despite the reopening of the culprit artery, distal microcirculation damage is frequent. Its pathogenesis is complex and multifactorial. In light of our study, patients likely to develop this phenomenon after primary coronary angioplasty can be predicted based on simple clinical and angiographic characteristics. In particular, elderly patients, delayed reperfusion times, low TIMI flow, and/or high thrombotic burden on initial angiography, as well as patients with long target lesions, are at increased risk of developing no reflow. Due to this complex pathogenesis, no single therapy is sufficiently effective. However, an approach combining multiple strategies and targeting risk factors should be implemented. Currently, there are no specific recommendations for therapeutic management, but numerous avenues are under investigation, both in the acute phase in the catheterization laboratory and from a pharmacological perspective.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest declared.

Statement of ethical approval

In accordance with COPE guidelines.

Statement of informed consent

The authors confirm that written consent for the submission and publication of this case, including the images, was obtained from the patient, in accordance with the guidelines of the Committee on Publication Ethics (COPE).

Availability of Data and Materials

Data sharing is not applicable to this article, as no datasets were generated or analyzed during this study.

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